TABLE 2.—Continued

Author, year, country	Population	Cough	Phlegm	Other		Comments
Higgins et al., 1977, U.S.	4,699 men and women, aged 20–74, Tecumseh			Chronic bronchitis		Chronic bronchitis (cough and phlegm ≥3 mo/yr); chronic bronchitis increased with age for male smokers; no age trend apparent for male or female nonsmokers; dose-response relationship between chronic bronchitis and cigarette smoking (age adjusted)
				Men		
				NS	5.1	
				EX	2.6	
				SM		
				<20/day	13.4	
				≥20/day	29.9	
				Pipe/cigar	8.4	
				Women		
				NS	3.5	
				EX	4.7	
				SM		
				<20/day	4.8	
				≥20/day	15.3	

TABLE 2.—Continued

Author, year, country	Population	Cough	Phlegm	Other	Comments
Lebowitz and Burrows, 1977, U.S.	2,857 men and women, aged 14-96, Tucson	Chronic cough and/or phlegm			Male prevalence consistently greater than female only in older age groups; frequency of symptoms increased with age; impossible to distinquish effects of aging and increased duration of smoking
		Men			
		NS	10.3		
		SM (pack years)			
		<6	29.0		
		6-20	35.8		
		21-40	47.9		
		41+	61.1		
		Women			
		NS	12.1		
		SM (pack-years)			
		<6	21.0		
		6-20	33.1		
		21-40	40.5		
		41+	60.4		

TABLE 2.—Continued

Author, year, country	Population	Cough	Phlegm	Other	Comments
Bland et al., 1978, Great Britain	6,320 first-year secondary school children, Derbyshire	Morning cough Boys NS 3.1 SM once 2.9 Occas. 4.0 1 per wk. 19.2 Girls NS 1.8 SM once 4.5 Occas. 6.0 1 per wk. 13.5 Cough at other times Boys NS 20 SM once 27 Occas. 34 1 per wk. 47 Girls NS 19 SM once 30 Occas. 35 1 per wk. 47		Breathlessness Boys NS 12 SM once 14 Occas. 22 1 per wk. 35 Girls NS 17 SM once 22 Occas. 29 1 per wk. 40	No questions on phlegm; child's smoking habits more important than parents' smoking habits; parents' smoking habits independently related to most symptom frequencies for boys and girls

TABLE 2.—Continued

Author, year, country	Population	Cough		Phlegm	Other		Comments
Huhti et al., 1978, Finland	1,162 men, aged 25–65, Hankasalmi	All day in winter		All day in winter	Chronic bronchitis		For total group, significant increase with age of cough, phlegm, and severe breathlessness; for nonsmokers, signficant increase with age for phlegm and breathlessness only
		Age	NS	NS	Age	NS	
		25–39	2	5	25–39	9	
		40–49	2	2	40–49	2	
		50–59	5	8	50–59	15	
		60–69	4	7	60–69	19	
		Age	EX	EX		EX	
		25–39	—	11	25–39	11	
		40–49	—	10	40–49	14	
		50–59	4	8	50–59	11	
		60–69	12	18	60–69	28	
		Age	SM	SM	SM 1-14 g/day		
		25–39	9	14	25–39	29	
		40–49	19	29	40–49	39	
		50–59	19	24	50–59	31	
		60–69	30	27	60–69	39	
					SM 15–24 g/day		
					25–39	13	
					40–49	45	
					50–59	46	
					60–69	46	
					SM $\geq$25 g/day		
					25–39	50	
					40–49	63	
					50–59	57	
					60–69	53	

TABLE 2.—Continued

Author, year, country	Population	Cough			Phlegm			Other			Comments
Manfreda et al., 1978 Canada	273 men and 229 women, aged 24–55, two communities in Manitoba	Most days ≥3 mo/yr			Most days ≥3 mo/yr			Wheeze apart from colds			No consistent difference in symptom prevalence for two communities; higher prevalence of cough, phlegm, and wheeze among smokers than nonsmokers or ex-smokers;
					Men						*CH=Charleswood
			CH*	PLP**		CH	PLP		CH	PLP	**PLP=Portage la Prairie
		NS	8.3	4.0	NS	—	4.0	NS	4.2	8.0	
		EX	8.1	2.9	EX	10.8	5.7	EX	10.8	14.3	
		SM	25.4	31.5	SM	16.9	24.7	SM	26.8	31.5	
					Women						
		NS	—	4.0	NS	—	4.0	NS	3.5	8.0	
		EX	—	10.0	EX	—	5.0	EX	12.1	20.0	
		SM	20.3	31.7	SM	10.2	25.4	SM	25.4	30.2	

TABLE 2.—Continued

Author, year, country	Population	Cough		Phlegm	Other	Comments
Rawbone et al., 1978, Great Britain	10,498 secondary school children, aged 11–17, Hounslow	A little most days		With colds	Frequent colds	*EXPER (ex-smokers and experimental smokers combined); sex differences not significant; nonstandard questions; higher symptom prevalence in younger children not explained
		Age	NS	NS	NS	
		11	26.4	22.8	36.0	
		13	16.7	25.3	32.3	
		15	13.4	24.5	34.3	
			EXPER*	EXPER	EXPER	
		11	20.5	32.3	42.2	
		13	17.3	31.2	36.1	
		15	11.3	29.6	36.3	
			SM	SM	SM	
		11	24.3	56.1	51.1	
		13	25.9	49.6	50.4	
		15	27.4	53.6	39.8	
		A little every day				
			NS			
		11	7.3			
		13	4.2			
		15	4.7			
			EXPER			
		11	7.0			
		13	4.7			
		15	3.5			
			SM			
		11	29.2			
		13	17.8			
		15	13.4			

TABLE 2.—Continued

Author, year, country	Population	Cough	Phlegm	Other	Comments
Bouhuys et al., 1979, U.S.	7,203 residents, aged 7–65+, three communities	Usual cough LE* AN** WI† Men NS 8 10 15 SM 27 32 34 Women NS 7 12 9 SM 13 17 24			Smoking significantly associated with cough, phlegm, wheeze, and dyspnea; prevalence increased significantly with age, slightly higher in urban community; women had lower prevalence of phlegm and higher prevalence of dyspnea than men *LE=Lebanon **AN=Ansonia †WI=Winnsboro
Burghard et al., 1979, France	29,138 students, aged 14–18, Bas-Rhin Department	Morning NS 13.7 SM 25.7 Day or night NS 16.9 SM 29.1 Chronic NS 2.7 SM 6.6		Breathlessness NS 14.1 SM 22.2	Prevalence of symptoms increased with increasing cigarette consumption; girls had higher prevalence of respiratory symptoms for each smoking category

TABLE 2.—Continued

Author, year, country	Population	Cough		Phlegm		Other		Comments
Gulsvik,	19,988 people,	Morning cough		When coughing		Cough and phlegm periods		Cough and phlegm increased more
1979,	aged 15–70,	NS	11	NS	10	NS	6	with age for smokers (10–19
Norway	Oslo	EX	15	EX	18	EX	8	cig/day) than nonsmokers; no
		SM	36	SM	28	SM	16	significant relationship between
		Daytime cough						age and prevalence of periods of
		NS	4					cough and/or phlegm;
		EX	7					dose–response relationship
		SM	16					between number of cigarettes and
		Cough 3 mos/yr						symptoms reported; data not
		NS	3					given
		EX	5					
		SM	14					
Liard et al.,	899 men and women,	Men						Respiratory symptoms (cough and/or
1980,	aged 20–60+,	NS	16.0					phlegm 3 mos/yr. for 2 years); not a
France	(av. 39), Paris	SM	25.4					random sample; male and female
		Women						smokers had similar symptom
		NS	8.1					prevalence; female nonsmokers had
		SM	26.5					lower prevalence

TABLE 2.—Continued

Author, year, country	Population	Cough	Phlegm	Other	Comments
Park,	856 university	Morning	Morning	Breathlessness on exertion	Symptom prevalences apparently
1981,	men and women,	NS 16.0	NS 20.1	NS 23.2	not age-adjusted; significance
Korea	aged 18–29,	EX 31.3	EX 22.9	EX 25.0	levels not reported; nonstand-
	Seoul	SM 34.0	SM 26.1	SM 29.7	ard questions; symptoms current
		Daytime	Daytime		
		NS 4.2	NS 2.1		
		EX 8.3	EX 14.6		
		SM 10.9	SM 12.0		
		Nightime	Nightime		
		NS 13.5	NS 7.3		
		EX 18.8	EX 10.4		
		SM 19.9	SM 13.2		
Neukirch et al.,	2,266 secondary	Usual cough and/or phlegm			21.8% of boys, 32.2% of girls
1982,	school students,	Boys			were current smokers; girl
France	aged ≤ 11–≥ 18	NS 26.1			smokers had higher symptom
	(mean 14.9),	SM 34.9			prevalence than boys if total
	Paris	Girls			lifetime cigarettes >4,000; results
		NS 26.9			probably not age adjusted
		SM 44.7			
Schenker et al.,	5,686 women,	Chronic cough	Chronic phlegm	Wheeze most days or nights	Cough and phlegm most strongly
1982,	aged 17–74 (mean	NS 5.6	NS 4.5	NS 7.2	related to current cigarettes/day;
U.S.	44.6), western	EX 7.5	EX 6.7	EX 8.3	tar content had independent
	Pennsylvania,	SM	SM	SM	effects; age effect seen for
	telephone interviews	1–14 9.1	1–14 7.2	1–14 14.4	nonsmokers, but not current
		15–24 17.0	15–24 16.7	15–24 18.5	smokers; symptom
		25+ 31.8	25+ 24.8	25+ 28.0	prevalences age adjusted

TABLE 3.—Prevalence (percent of cough, phlegm, and other symptoms for nonsmokers (NS), smokers (SM), and ex-smokers (EX), longitudinal studies

Author, year, country	Population	Smoking habits		Symptoms				Comments
Ferris et al., 1976, U.S.	1,201 men and women, aged 25–74 in 1961, Berlin New Hampshire			Cough		Phlegm		72.3% of men, 78.4% of women followed up; 1973, symptom prevalences, age adjusted to compare with 1967, showed little change
		1973		1967	1973	1967	1973	
				Men				
		NS		6.0	8.5	8.9	7.6	
		EX		20.5	9.7	23.3	15.9	
		SM						
		1–14		22.2	25.5	17.9	27.5	
		15–24		35.4	26.5	31.8	30.0	
		25–34		26.1	25.7	33.8	32.4	
		35+		50.6	56.4	37.1	51.9	
				Women				
		NS		4.4	6.2	8.1	7.4	
		EX		3.2	5.2	7.3	10.1	
		SM						
		1–14		10.7	10.0	11.6	9.8	
		15–24		19.5	16.3	21.8	9.8	
		25–34		27.2	16.1	22.5	21.8	
		35+		44.7	31.0	43.1	41.2	
Kiernan et al., 1976, Great Britain	2,738 men and women, aged 25, born in 1946, exams in 1966 and 1971			Cough day or night in winter				Effects of chest illness before age 2, father's vocation, and current smoking significant; air pollution effect not significant; current smoking had largest effects * Prevalence, 1966 vs. 1972, $p < 0.05$
		1966	1971	1966		1971		
		NS	NS	5.5		4.9		
		NS	SM	7.2		9.6*		
		SM	SM	14.3		18.5*		
		SM	EX	9.2		5.8		

TABLE 3.—Continued

Author, year, country	Population	Smoking habits		Symptoms				Comments
Leeder et al.,	2,130 fathers,			Cough/phlegm prevalence range				In male ex-smokers, prevalence
1977,	mean age 31.0±6.1,			Men				of cough/phlegm decreased
Great Britain	2,148 mothers,	1st period	2nd period	1st 3-yr period	2nd 3-yr period			over time; no significant
	mean age 27.9±5.3,	NS	NS	8.6–9.6	9.2–11.1			change in prevalence in female
	children born	NS	SM	4.8–16.9	13.3–20.5			ex-smokers, but numbers
	1963–1965,	SM	SM	25.6–30.2	30.8–34.0			were small
	London, 6 year	SM	EX	21.8–25.3	5.8–20.7			
	followup			Women				
		NS	NS	4.9– 6.8	5.8– 7.3			
		NS	SM	8.2–10.2	13.3–18.4			
		SM	SM	16.3–22.4	23.0–28.4			
		SM	EX	4.1–22.5	12.2–14.3			
Woolf and Zamel,	302 women, aged			Cough and/or phlegm		Breathlessness		60% followed up; all subjects
1980,	25–54 at initial			1st exam	Final exam	1st exam	Final exam	maintained consistent smoking
Canada	study, 5-year	NS		10	14	10	5	habits for 5 years
	followup	EX		3	13	18	8	
		SM		56	54	25	21	

TABLE 3.—Continued

Author, year, country	Population	Smoking habits		Symptoms				Comments
				Usual cough		Usual phlegm		
		1972	1978	1972	1978	1972	1978	
Beck et al., 1982, U.S.	1,262 white residents, aged 7–55+, Lebanon, Connecticut, exams in 1972 and 1978			Men				55% followed up; health indices of respondents and non-respondents similar; symptom prevalence tended to decline, but few changes were significant; * Prevalence, 1972 vs. 1978, p <0.5
		NS	NS	5	2	7	3	
		NS	SM	0	0	0	4	
		SM	SM	23	21	22	26	
		SM	EX	25	2*	18	8	
		EX	EX	7	6	12	15	
				Women				
		NS	NS	7	4	5	6	
		NS	SM	0	0	0	9	
		SM	SM	20	14	15	11	
		SM	EX	28	12	8	16	
		EX	EX	10	3	4	1	

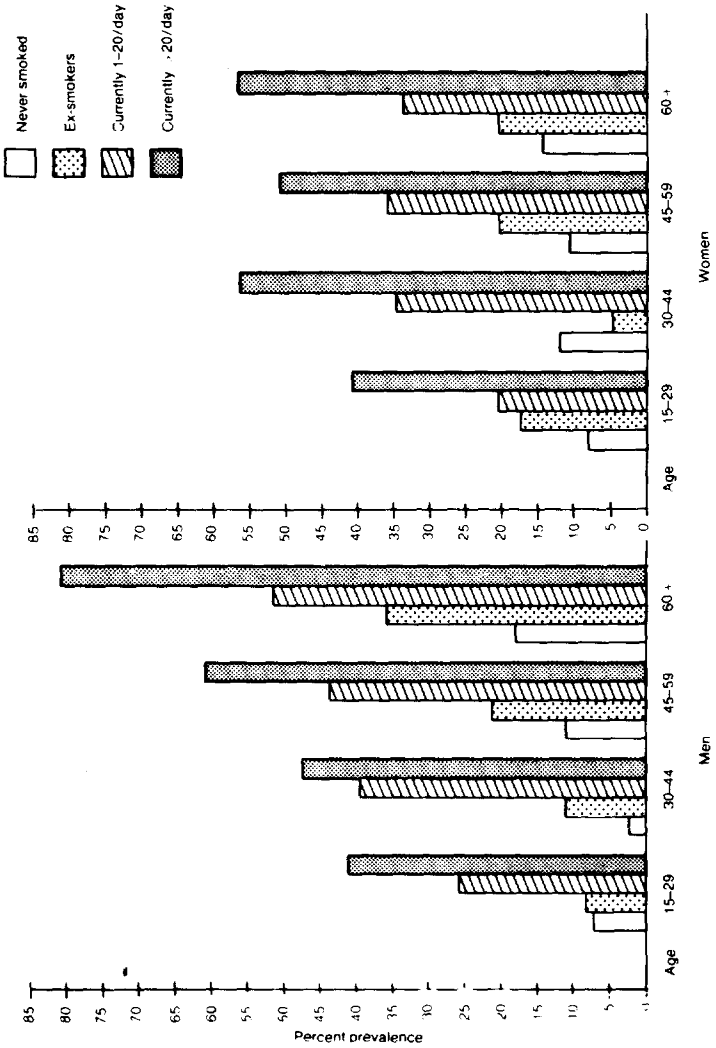

FIGURE 11.—Prevalence of chronic cough and/or chronic sputum among samples of men and women in Tucson, Arizona

SOURCE: Lebowitz and Burrows (1977).

Dose-Response Relationships

The most common measures of dose are the number of cigarettes currently smoked per day and the pack-years of cigarette consumption; the latter estimates lifetime exposure by integrating the number of cigarettes smoked (by pack) and the duration of cigarette use. Errors of memory compromise the accuracy of retrospective information, which may also be biased by differential recall in those

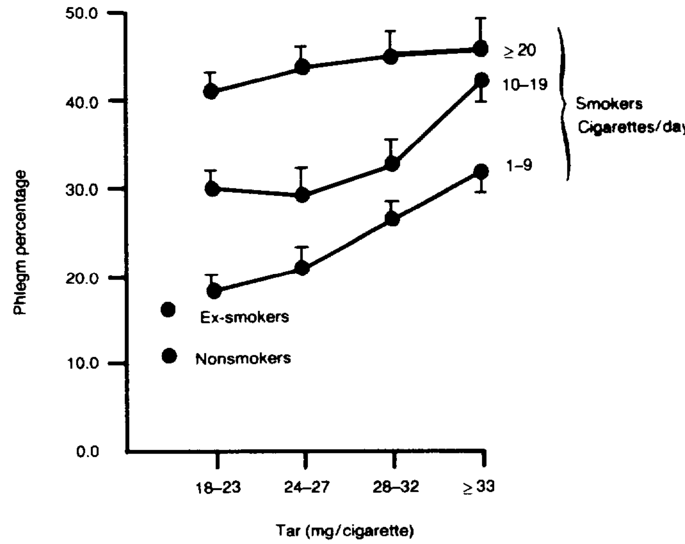

FIGURE 12.—Percentage of smokers with phlegm production (adjusted for age), according to tar yield of cigarettes

SOURCE: Higenbottam et al. (1980).

with and without smoking-related symptoms or diseases. Even accurate reports of current smoking habits fail to take into account all the sources of variation in exposure associated with the material used in cigarette manufacture or generated in the burning of cigarettes. The dose of noxious materials received is also influenced by human behavior, including the number, volume, and timing of puffs taken with each cigarette; retention of smoke in the mouth; depth of inhalation; disposition of the cigarette between puffs; and other aspects of smoking style that are not reproduced by the smoking-machines used to measure tar and nicotine yield.

Prevalence rates of cough or phlegm, or both, generally increase as the number of cigarettes smoked per day increases. The trends illustrated in Figures 11 and 12 were present in both sexes and all age groups (Lebowitz and Burrows 1977; Dean et al. 1978; Higgins et al. 1977; Huhti et al. 1978; Higenbottam et al. 1980; Schenker et al. 1982). Bland et al. (1978) found a dose–response relationship in secondary school children, among whom rates of reporting cough were higher in those who smoked most, even though levels of cigarette consumption were generally reported to be low. At the other extreme of the age range the trend is also apparent, even though symptomatic smokers are more likely than asymptomatic smokers to stop smoking or to reduce their cigarette consumption

(Higgins 1974; Fletcher 1976). Symptoms were more prevalent among heavier smokers of filter cigarettes as well as of nonfilter cigarettes (Dean et al. 1971). Prevalence rates of cough, phlegm, chronic bronchitis, and mucus hypersecretion show a similar pattern of association with pack-years of exposure (Tager and Speizer 1976; Lebowitz and Burrows 1977). Rates of incidence and remission observed in longitudinal studies add further support to the strong evidence that respiratory symptoms increase as exposure to cigarette smoke increases (Table 3).

In their study of more than 18,000 male civil servants in London, Higenbottam and colleagues (1980) found that the percentage of smokers who produced phlegm increased with increased daily cigarette consumption and also with increasing tar content of cigarettes among those who smoked less than 20 cigarettes a day. Symptoms were prevalent about equally among smokers of 20 or more cigarettes per day, regardless of the tar yield of the brands they used (Figure 12).

Schenker et al. (1982) reported the relationship of tar content of cigarettes to respiratory symptoms in a cross-sectional telephone survey of 5,686 adult women in rural Pennsylvania. The risk of chronic cough and phlegm was more strongly affected by the number of cigarettes smoked per day than by tar content. Cough and phlegm were reported least often by never smokers and with increasing frequency as the number of cigarettes smoked per day increased. Tar content of cigarettes was significantly associated with symptoms of chronic cough and phlegm—especially cough—and its effects were independent of the number of cigarettes smoked per day in a multiple logistic analysis. The risk (relative odds) of chronic cough for smokers of high tar cigarettes (20 or more mg) was approximately twice that for smokers of an equivalent number of low tar cigarettes (10 or less mg). A limitation of this cross-sectional study was the determination of tar content for current cigarettes only, rather than for lifetime smoking habits. Although the apparent relationship between tar content and symptoms could have been caused by changes in smoking habits, this was considered unlikely because symptomatic smokers tend to reduce their consumption of cigarettes more than asymptomatic smokers (Fletcher et al. 1976) and may also switch to low yield cigarettes. In this situation, any reported effect of tar content on symptoms would be an underestimate.

In summary, the prevalence of symptoms increases with dose of smoke exposure, when dose is measured by number of cigarettes smoked per day or tar content of the cigarette smoked.

Relationship of Cough and Phlegm to Sex and Age

Prevalence rates of cough and phlegm ascertained in epidemiological studies generally increase with age and are higher in men than in women, as shown in Figure 11 and Tables 2 and 3. Rates also vary with smoking habits. Rates in nonsmokers better clarify associations of symptoms with age and sex than do rates in smokers, since they are less confounded by variations in exposure to cigarette smoke. However, recent evidence linking passive smoking with increased prevalence of respiratory symptoms suggests that rates in nonsmokers may be in excess of those that would be found in a population completely free of exposure to cigarette smoke (Lefcoe et al. 1983; Weiss et al. 1983).

Rates of reporting cough or phlegm or both were roughly equal in nonsmoking men and women in several cross-sectional studies (Bland et al. 1978; Higgins et al. 1977; Lebowitz and Burrows 1977; Manfreda et al. 1978; Neukirch et al. 1982; Rawbone et al. 1978). Rates were higher in nonsmoking men in some populations (Dean et al. 1977; Liard et al. 1980; Tager and Speizer 1976). Bouhuys et al. (1979) found no sex difference in the prevalence of cough, but a higher rate of reporting phlegm in male nonsmokers (Table 2). In most of these studies, the rates were not corrected for exposures to other respiratory irritants in the workplace or in the general environment.

In general, symptoms are more prevalent in male smokers than in female smokers (Table 3). However, differences in prevalence rates between the sexes are generally smaller or absent when comparisons are made between men and women who smoke similar numbers of cigarettes. Lebowitz and Burrows (1977) found that the excess prevalence of symptoms in male smokers compared with female smokers tended to be greatest at older ages, where there are also the greatest differences in smoking behavior. Men in these birth cohorts tend to have begun smoking earlier in life, smoke more cigarettes per day, inhale more deeply, and smoke higher tar and nicotine or unfiltered cigarettes. Two studies from France, Burghard et al. (1979) and Neukirch et al. (1982), concentrated on high school students. In general, the prevalence of smoking was similar for both boys and girls for the two studies, although the Neukirch group found a somewhat higher rate among the girls (46 percent versus 39 percent). Slightly more boys than girls, however, smoked more than 10 cigarettes per day. In these two studies, the prevalence of symptoms was higher among female smokers than among male smokers. These data suggest that the past differences in prevalence of symptoms between the sexes is largely attributable to differences in cigarette consumption. These differences were substantial in the past, and are still present among older adults, whereas current smoking practices are about the same in male and female adolescents and young adults.

Prevalence rates of cough, phlegm, and chronic bronchitis increased with increasing age in the U.S. population samples studied by the National Center for Health Statistics (1981) and in several of the cross-sectional studies cited in Table 2. However, differences in rates of reporting symptoms among people of different ages may relate to effects of aging, differences in current exposures, or differences in exposure to cigarette smoke or other noxious agents in the past. It is therefore difficult or impossible to use cross-sectional data to separate effects of aging from effects of duration, dose, and nature of cigarette smoke exposure throughout life. Longitudinal studies provide information on time trends, both in exposure and in onset and course of disease. Nevertheless, conclusions may be incorrect if people who drop out of longitudinal studies are different from those who continue to participate.

Prevalence of symptoms increased with increasing age among men in cross-sectional data from Tucson (Figure 11), but the trend was more apparent among smokers and ex-smokers than among nonsmokers. However, Lebowitz and Burrows (1977) could not distinguish between an association caused by increasing age and an association due to increasing duration of exposure to cigarette smoke in smokers because the two were so highly correlated. Among women, symptoms were reported more frequently at ages 30 to 44 than at ages 15 to 29 (except by ex-smokers), but prevalence rates were essentially the same for the three groups over age 30. Higgins et al. (1977) found that there was no increase in cough and phlegm with increasing age in male or female nonsmokers in Tecumseh (Michigan), whereas prevalence rates increased with increasing age in male smokers. The pattern in female smokers was similar to that in Tucson and showed an increase with age up to age 30 or 40, but rates declined with increasing age after age 50. The extent to which these patterns related to amount smoked or duration of smoking was not reported, but these older birth cohorts of women probably began to smoke later in life and smoked fewer cigarettes per day, according to national smoking survey data.

In other cross-sectional studies cited in Table 2, symptom prevalence increased with age in the populations studied (Bouhuys et al. 1979; Dean et al. 1977; Gulsvik 1979; Huhti et al. 1978; Tager and Speizer 1976), but the trend was noted by Gulsvik to be less in nonsmokers. Huhti et al. found a significant increase with age among nonsmokers for phlegm and dyspnea only. Schenker et al. (1982) observed a trend for nonsmokers but not for smokers, and Tager and Speizer found that adjusting for smoking eliminated the trend with age.

Prevalence rates of cough and phlegm on two occasions 3 to 6 years apart are shown in Table 3 for five recent longitudinal studies of populations in the United States, Canada, and Great Britain. Kiernan et al. (1976), Leeder et al. (1977), Woolf and Zamel (1980), and Beck et al. (1982) found little change in the prevalence of symptoms among continuing nonsmokers during the followup interval of up to 6 years. The rates among nonsmokers reported by Ferris et al. (1976) are similar on the two occasions, but symptoms were presented by smoking habits at followup only, and any effect of age was deliberately adjusted out because the authors' purpose was to evaluate effects of changes in smoking, changes in pollution, and trends over time independent of changes in age. Cough and phlegm appeared to be more frequent at followup in the persistent smokers studied by Kiernan et al. (1976) and Leeder et al. (1977), and about the same in women studied by Woolf and Zamel (1980) and in men studied by Beck et al. (1982). However, rates were slightly lower at followup in the female smokers followed by Beck. Even though starting to smoke or quitting can be eliminated as the explanation for increases or decreases in symptom prevalence over the course of these studies, it is possible that changes in the number or type of cigarettes smoked by persistent smokers influenced the prevalence of symptoms. The duration of followup in all these studies was relatively brief, and it is still difficult to distinguish between effects of aging and effects of duration, amount, and nature of exposure to cigarette smoke in smokers, even when major changes in smoking behavior are controlled. However, available data suggest that age itself is not the major factor responsible for differences in the frequency or distribution of symptoms in populations of nonsmokers and smokers.

Relationship of Cough and Phlegm to Airflow Obstruction

Many cross-sectional studies have found associations between cough, phlegm, chronic bronchitis, or mucus hypersecretion and reduced levels of pulmonary function. The forced expiratory volume at 1 second (FEV_1) has been measured in most clinical studies and in nearly all epidemiological studies, and mean levels of FEV_1 are generally slightly lower in groups of people who report respiratory symptoms (USPHS 1964, 1971; USDHEW 1979; USDHHS 1980a, 1981). Recent studies have compared other measures of pulmonary function in people with and without symptoms and have provided longitudinal data on pulmonary function for symptomatic and asymptomatic smokers and nonsmokers. Attention has been given to understanding the natural history of chronic airways obstruction and the interrelationships of respiratory symptoms, levels and rates of decline of pulmonary function, and their independent and interrelated associations with cigarette smoking. Several investigators have emphasized the desirability of identifying in advance those smokers who will develop severe COLD; symptoms and other characteristics have been evaluated as potential predictors of morbidity or mortality from COLD.

Fletcher and colleagues (1976) found that the age–height standardized FEV_1 at the initial survey of their population of working men in London was inversely related to the volume of sputum produced in the first hour after getting up. The regression of FEV_1 on age, given height, was steeper for symptomatic cigarette smokers than for asymptomatic smokers or nonsmokers. However, the authors caution that men may develop symptoms as they age and change from one regression slope to the other.

Burrows et al. (1977a) found that an index of cough or sputum was related to FEV_1 percent predicted when pack-years of smoking were controlled in a multiple regression analysis. Regressions of FEV_1 percent predicted on pack-years are shown for people with and without chronic cough and sputum in Figure 13; the intercept at 0 pack-years was lower and the decline in FEV_1 with increasing pack-years was significantly greater for those with chronic cough and sputum than for those with no cough or sputum. The authors calculated that values of FEV_1 were lower by about 10 percent in people with cough and sputum, regardless of smoking habits, and that values declined by about 4 percent of predicted for each 10 pack-years of smoking in people with cough and sputum and by about 2 percent in subjects without productive cough. There was a significant relationship between FEV_1 and pack-years of smoking in asymptomatic smokers in this population. A weaker relationship between cough and sputum and $\dot{V}_{max\,25\%}$ was also found to be independent of pack-years of smoking; however, prediction equations for flow rates have been revised substantially (Knudsen 1983), and the extent to which relationships between the revised flow rates and pack-years of smoking differ in symptomatic and asymptomatic subjects has not been reported.

Dosman et al. (1976) found poor correlations between respiratory symptoms and dynamic lung compliance, closing volume, closing capacity, slope of phase III, and helium flow-volume curves in a study of 49 smokers and 60 nonsmokers who were recruited from a smoking cessation clinic, a personnel department, and the staff of a laboratory.

In their community-based studies of children and adults, Bouhuys and colleagues (1977) studied relationships between respiratory symptoms and loss of lung function in smokers and nonsmokers. They found that residual values (observed–predicted) of FVC, FEV_1, PEF, $MEF_{50\%}$, and $MEF_{25\%}$ were not significantly different in people with no symptoms or only one symptom when analyses were done separately for adult white male smokers and nonsmokers. When a symptom score was used to combine information on usual cough, usual phlegm, wheeze, and dyspnea, decrements in lung function were greatest among those with most symptoms.

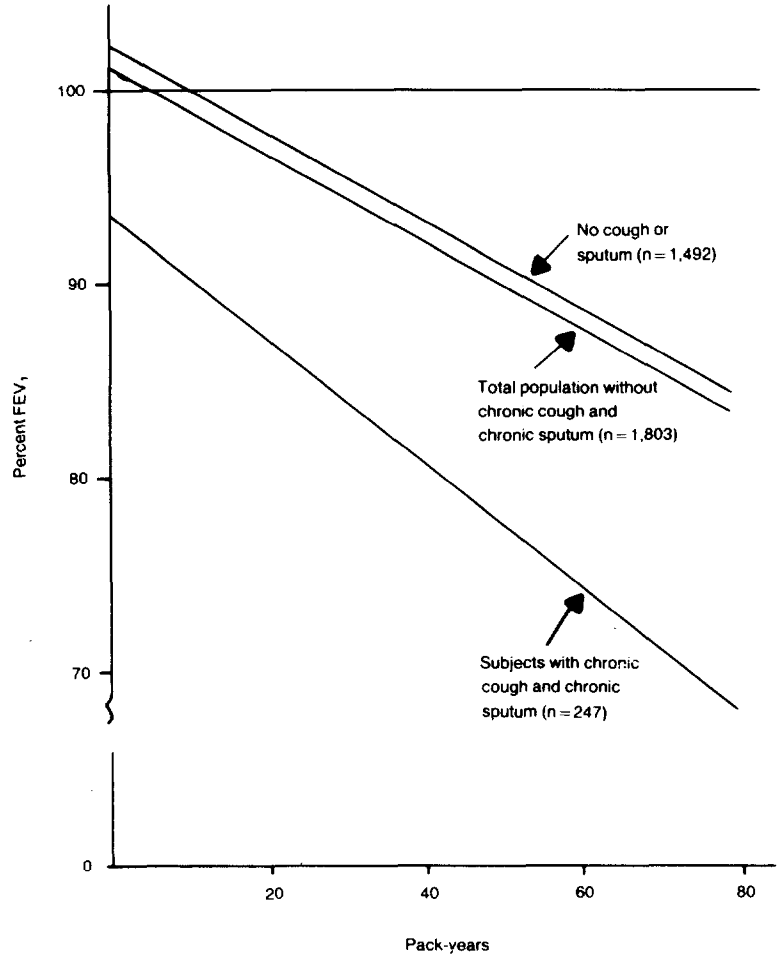

Figure 13.—Percentage distribution of predicted forced expiratory volume in 1 second (FEV_1) versus pack-year of cigarettes smoked, by cough and sputum history

SOURCE: Burrows et al. (1977a).

In a study (Detels et al. 1982) designed to assess the relative sensitivity and specificity of symptoms, the flow-volume curve (FV), the single breath nitrogen test (SBNT), and specific airway conductance (S_{Gaw}) for identifying COLD were compared with the FEV_1/FVC ratio and with one another in 1,201 residents of Los Angeles 25 to 29 years old. The tests were done in 1978–1979 at a followup examination of a previously defined cohort. Prevalence rates of cough and sputum were 9 percent in never smokers, 26 percent in current smokers, and 33 percent in smokers of 20 or more cigarettes a day. Prevalence rates of an abnormal FEV_1/FVC ratio in these groups were 8, 23, and 33 percent, respectively (the FEV_1/FVC ratio was considered abnormal if it was below the 95th percentile for never smokers without a history of respiratory illness). The researchers found that there was very little overlap between the presence of productive cough and abnormal tests, and that none of the tests of function showed reasonable concordance with this symptom. Lack of reasonable concordance meant that none of the other tests were abnormal in 50 percent or more of the individuals with productive cough. In this study, the FEV_1/FVC ratio was used as the standard against which the sensitivities of the other tests were judged; the sensitivity of the FEV_1/FVC itself was evaluated by its agreement with those tests found to be sensitive in the study. The lack of an independent method for identifying COLD, the cross-sectional nature of these data, and the way in which analyses were done restrict the ability to make biological inferences about the independence of the effects of cigarette smoking that lead to cough and sputum or to chronic airflow limitation. However, the authors note their findings are consistent with the hypothesis that effects of smoking on cough and sputum are independent of effects on airflow limitation.

Insights into the course and pathogenesis of COLD have been developed by Fletcher and his colleagues from observations made during their 8-year longitudinal studies of levels and rates of decline in lung function in middle-aged working men in London (Fletcher 1976; Fletcher et al. 1976). These investigators found that various measures of sputum production were correlated with FEV_1 standardized for height and age, and that this correlation was weakened only slightly by adjusting for smoking habits. The researchers maintained that the association between sputum production and pulmonary function could be due entirely to a common causation. Some men with mucus hypersecretion had normal FEV_1; conversely, some men with airflow obstruction did not report phlegm. Nevertheless, the relationship between phlegm and reduced FEV_1 was strong enough to give rise to an estimated reduction in FEV_1 of about 0.1 liters for every ml of sputum expectorated in the first hour after getting up. However, because decline in FEV_1 (FEV_1 slope) was not related to measures of sputum production when level of FEV_1 and smoking habits were controlled, the researchers concluded that mucus hypersecretion is not a cause of accelerated decline in FEV_1. Furthermore, there was no evidence that short-term changes in sputum production were associated with short-term changes in FEV_1. The researchers concluded that the association between expectoration and reduced FEV_1 is caused by the increased susceptibility of some people to both expectoration and excessive loss of FEV_1 when they are exposed to cigarette smoke or, presumably, to other noxious materials. This study has made important contributions to understanding the natural history of chronic bronchitis and emphysema, but the duration of followup was only 8 years, the men were 30 to 59 years of age at the start of the study, and their mean age was 51 years at the midpoint. Similar studies of younger men and women and observations over longer periods of time are needed to extend these findings.

Johnston et al. (1976) found that sputum volume was not related to decline in FEV_1 in a 10-year followup study of chronic bronchitic patients. There was no difference in sputum volume between patients whose FEV_1 fell by more than 33 percent and controls (matched on initial FEV_1) whose FEV_1 did not fall. Furthermore, sputum volume was reduced in response to stopping smoking or to antibiotic treatment, whereas rate of decline of FEV_1 was unaffected. In this and other studies (Higgins et al. 1970; Fletcher et al. 1976; Peto et al. 1983) FEV_1 was strongly predictive of morbidity and mortality, whereas respiratory symptoms were not.

Woolf and Zamel (1980) studied "normal" employed women aged 25 to 54 in a longitudinal study designed to identify smokers at increased risk of developing COLD. Ventilatory function was measured at the beginning and at the end of a 5-year period during which smoking habits and symptoms were ascertained annually. Differences between initial and followup values of pulmonary function tests were expressed as a percentage of the initial value and compared in persistent nonsmokers and persistent smokers who either consistently reported or consistently denied cough or sputum. The decline in FEV_1, FEV_1/FVC, and $FEF_{25-75\%}$ was greater in symptomatic smokers than in asymptomatic nonsmokers, but not significantly different in asymptomatic smokers compared with either nonsmokers or symptomatic smokers. The average number of cigarettes smoked during the course of the study was greater for smokers with cough and sputum. Change in $FEF_{25-75\%}$ was evaluated in individual smokers, and no association was detected between cough and sputum and percentage change in this measure of lung function. The investigators identified one group of smokers whose decline in $FEF_{25-75\%}$ was similar to that in nonsmoking women and another group with a greater decline; cigarette consumption was similar in the two groups. The investigators concluded that individual susceptibility is an important determinant of the effect of cigarette smoking, because some women develop symptoms and others remain symptomless but experience rapid worsening of ventilatory function. However, they noted a tendency for both cough and sputum and rapid worsening of ventilatory function to coexist. The number of women in some groups was very small, and the measure of decline in lung function used by these researchers does not take into account regression to the mean or assess absolute reduction; those with smaller initial values will have greater percentage reductions for a constant absolute reduction in function.

Followup studies at 10 and 15 years of the Tecumseh, Michigan, population showed that incidence rates of obstructive airways disease were higher in men and women who reported cough, phlegm, or both symptoms (chronic bronchitis) at entry compared with those who denied these symptoms (Figure 14) (Higgins et al. 1982). Both cough and chronic bronchitis were significant predictors of obstructive airways disease in men even when smoking habits were controlled in multiple logistic analyses. However, respiratory symptoms were poorer predictors of impaired pulmonary function at followup than were smoking habits and baseline levels of lung function. In a multiple logistic model with age, smoking habits, and level of lung function as risk factors, over 60 percent of the 10-year incidence cases developed among men and women in the top 10 percent of the risk distribution, whereas only 36 percent of incidence cases were in the top decile of risk when cough, rather than FEV_1, was used as a risk factor (Higgins 1984).

Summary

Cigarette smoking is associated with respiratory symptoms, including mucus hypersecretion, and with prevalence and incidence of COLD manifested by irreversibly impaired pulmonary function. While some smokers develop both conditions, and those with cough and phlegm are at increased risk of developing airways obstruction, the conditions can occur separately by mechanisms that are imperfectly understood but appear to be different. The excess risk of reduced FEV_1 or COLD in symptomatic smokers compared with asymptomatic smokers may be a reflection of increased susceptibility in some individuals. However, it may also be a measure of increased dose of cigarette smoke, in that smokers who report cough and phlegm tend to smoke more heavily than smokers who deny these symptoms, and measures such as numbers of cigarettes smoked per day are not precise enough to control adequately for the amount of smoke exposure. The rate, number, and volume of puffing as well as the depth of inhalation can vary substantially between smokers and are important additional measures of cigarette smoke exposure dose.

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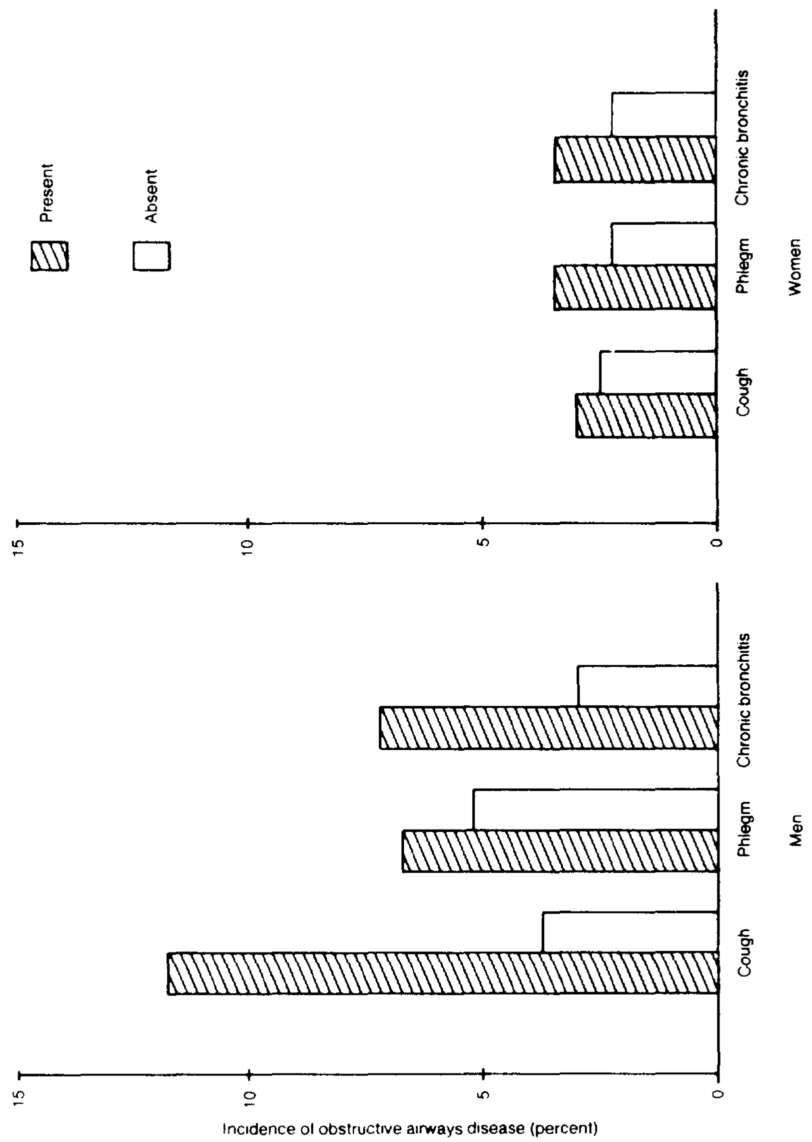

FIGURE 14.—Age-adjusted 15-year incidence of obstructive airways disease, by cough, phlegm, and chronic bronchitis status at entry to the study, Tecumseh, ages 16 to 64, 1962–1979

SOURCE: Higgins et al. (1982).

CHRONIC AIRFLOW OBSTRUCTION

Introduction

Airflow obstruction is the physiological consequence of disease processes that narrow the airway. In asthma the obstruction is reversible with pharmacologic bronchodilation, whereas the obstruction associated with airways damage and emphysema is often not reversible. The terminology with regard to permanent airflow obstruction has varied. The 1958 Ciba Foundation Guest Symposium proposed "generalized obstructive lung disease," which was subdivided into "asthma" and "irreversible or persistent obstructive lung disease" (1959); in the 1962 recommendations of the American Thoracic Society, "chronic obstructive bronchitis" was the only definition that mentioned abnormality of expiratory flow (American Thoracic Society 1962). In 1975, a joint committee of the American College of Chest Physicians and the American Thoracic Society recommended the term "chronic obstructive pulmonary disease" (American College of Chest Physicians and American Thoracic Society 1975). Thurlbeck (1976, 1977) has advocated the use of "chronic airflow obstruction," a functionally based definition that does not specify the underlying disease processes. Previous Reports of the Surgeon General have used varying terminology, including "chronic bronchopulmonary disease" in 1964, "chronic obstructive bronchopulmonary disease" in 1971, and "chronic obstructive lung disease" in 1979 (USPHS 1964, 1971; USDHEW 1979).

These definitions, however, cannot be readily applied to identify specific populations. Physiologists, epidemiologists, and clinicians often use differing approaches in determining whether airflow obstruction is present (Fletcher 1978). Physiologists, with the capability for making sophisticated laboratory measurements of airflow obstruction, may regard subtle early abnormalities of flow as definitive. In the community, epidemiologists have generally used spirometry as the primary method for assessing airflow obstruction. For epidemiologic purposes, airflow obstruction is usually defined by a forced expiratory volume in 1 second (FEV_1) less than a particular level after standardization for sex, age, and height, or by a ratio of the FEV_1 to the forced vital capacity (FVC) below a specified value. Tests of forced exhalation, such as the FEV_1, have the advantage of sensitivity to abnormalities of both the lung parenchyma and the airways (Mead 1979). Clinicians are more likely to detect and diagnose airflow obstruction when it is advanced and symptomatic. As would be anticipated, the differing approaches of physiologists, epidemiologists, and clinicians may lead to differing estimates of the frequency of airflow obstruction.

The natural history of chronic airflow obstruction in adults has been partially described by several recent prospective investigations: